COMBINATION PRODUCTS
DEVICE SPECIALISTS®

Inspection Readiness Support

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Inspection Readiness Support for:
• Pre-Inspection • PAI (Pre-Approval Inspection) • Post-Inspection

Do you expect inspection from FDA, EMA, MHRA and PIC/S?

Regulatory inspections can be a source of stress and uncertainty for many organizations. However, by understanding and preparing for these inspections, you can turn them into opportunities to demonstrate your commitment to quality and compliance.

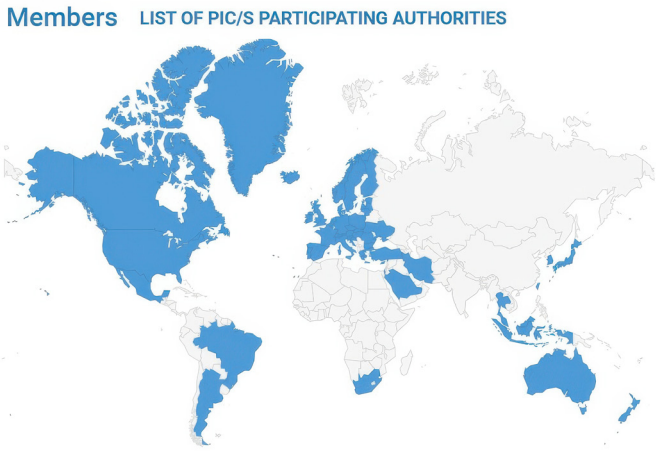
The FDA, EMA, MHRA, and PIC/S are increasingly harmonizing their inspection processes and expectations, reducing differences and simplifying preparation for organizations operating in multiple regions.

Regulatory authorities are increasingly emphasizing Quality Culture and Quality Management Maturity during inspections, recognizing their importance for ensuring product safety and efficacy.

Quality Culture is the shared values and practices that reflect an organization's commitment to quality. It involves prioritizing quality at all levels, promoting proactive problem-solving, continuous improvement, and open communication about quality issues.

Quality Management Maturity entails developing and implementing advanced quality management practices. It reflects an organization's progression from basic compliance to an integrated approach characterized by well-defined processes, effective risk management, and data-driven continuous improvement.

Organizations should prioritize Quality Culture and Quality Management Maturity in their preparation efforts. This approach not only meets regulatory expectations but also enhances operational efficiency and product quality.



Be the best & save Big

CPDS has developed an extensive series of trainings and services specifically designed for the unique needs of Pharma combination product manufacturers and their suppliers. With 30 years of proven and mature methods, CPDS guarantees that when these methods are followed and applied, Quality Management will become:

- Robust
- Efficient
- Mature
- Globally harmonized

Ultimately, this will create a lean GMP (Good Manufacturing Practice) system.

Pre-inspection readiness

Good inspection readiness should align with the quality culture of your daily operations. Companies with a mature GMP system don't really "prepare" for inspections—they operate in a constant state of readiness. This entails:

- Maintaining documentation
- Following lean processes and procedures
- Ensuring employees are well trained
- Addressing issues promptly as part of normal operations

Your goal should be that any investigator could walk in any day and find an inspection-ready operation. This means having systems that make quality the default state, rather than a special effort.
At CPDS, we have developed a lean, process-based cGMP approach. We work with you to analyze and help achieve that everyday readiness lean state. Did you know that this readiness state can significantly reduce your quality costs?

Time available before inspection

One year:

Depending on your needs, you have ample time for the transition to Maturity of Quality Management. By following the CPDS program, you can ensure that all your process owners create a high level of control. Remember, receiving external inspections is not just about the inspection day itself—it's an ongoing process involving meticulous documentation and quality records.
This period allows you to:

- Develop and refine your Quality Management System
- Train and align your team on best practices
- Ensure all processes are well-documented and controlled
- Conduct internal audits to identify and address any gaps
- Foster a culture of continuous improvement and readiness

Following these steps will not only help you prepare for inspections but also enhance the overall efficiency and quality of your operations.

Six months:

Depending on your needs, there is sufficient time for a compact program. During this period, the external support team may be expanded by bringing a few experts on board, identified by our partner staffing organization, and awaiting your approval.

This approach allows you to:

- Implement a focused and efficient Quality Management System
- Train your team on key inspection readiness practices
- Ensure critical processes are well-documented and controlled
- Conduct target internal audits to address potential immediate gaps
- Leverage the expertise of additional specialists to enhance your readiness

By following this strategy, you can maximize your preparation efforts and ensure a high level of inspection readiness within a shorter timeframe.

Two months:

Don't try to pack years of work into weeks and don't panic.
Instead, prepare your organization for the inspection with a solid process guideline. Here are some key steps:

- Train Your Staff: Ensure everyone knows their roles and responsibilities during the inspection
- Prepare Rooms, Hardware, and Protocols: Make sure all physical and digital resources are ready and functioning
- Organize Your Documentation and Quality Records: Have all necessary documents and records without mistakes
- Know Your Strong and Weak QMS Elements: Be aware of your Quality Management System's strengths and areas for improvement
- Learn to Communicate During Inspections: Be honest, precise, and personable when interacting with inspectors

By following these steps, you can achieve a state of readiness that will impress any investigator. If you need further guidance or assistance, feel free to reach out!

PAI

A Pre-Approval Inspection (PAI) is conducted, e.g.; by the FDA, only to ensure that a manufacturing establishment named in a drug application is capable of producing a drug and that the submitted data are accurate and complete. Here are the key objectives:

Objective 1: Readiness for Commercial Manufacturing:

Assess whether the establishment(s) has a quality system designed to achieve sufficient control over the facility and commercial manufacturing operations.

Objective 2: Conformance to Application:

Verify that the formulation, manufacturing or processing methods and analytical methods align with the descriptions in the CMC section of the application for the biobatch (and other pivotal clinical batches, when applicable), the proposed commercial scale batch and the API(s).

Objective 3: Data Integrity Audit:

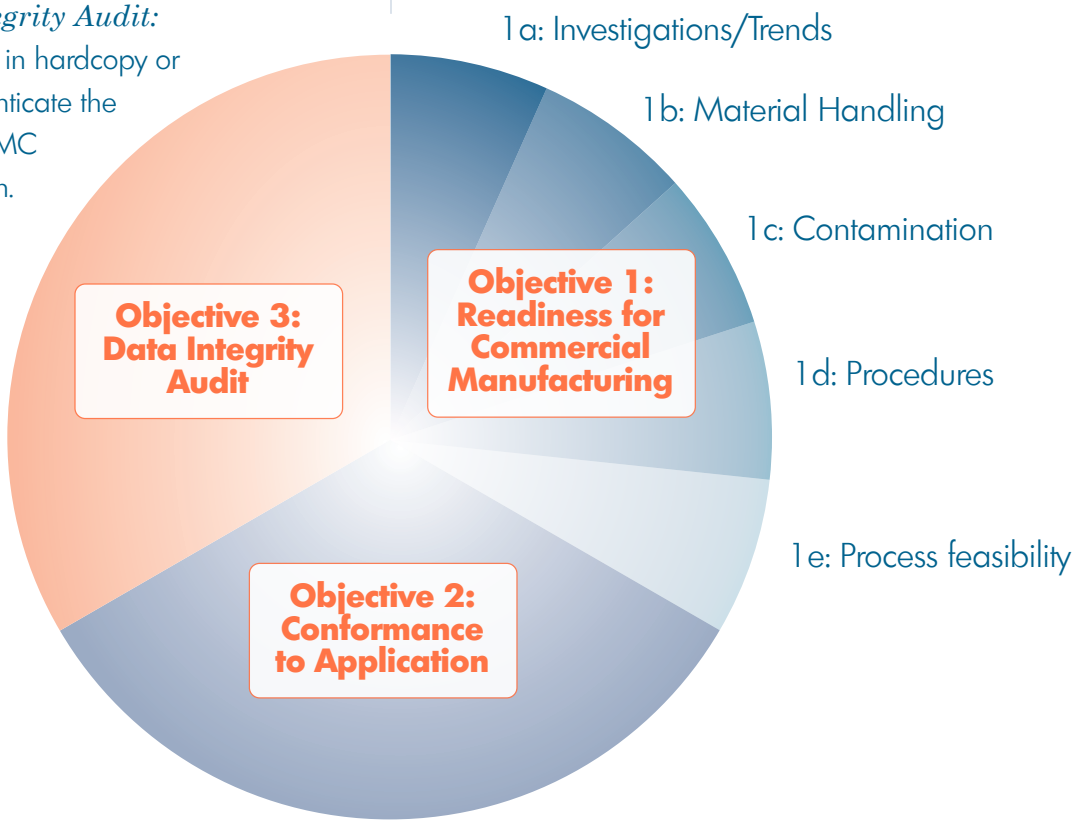
Audit raw data, whether in hardcopy or electronic form, to authenticate the data submitted in the CMC section of the application. Ensure that all relevant data (e.g., stability, biobatch data) were submitted in the CMC section, allowing CDER product reviewers to rely on the data as complete and accurate.

Outcome of the PAI inspection

Is there anything specific you'd like to discuss or expand on regarding PAIs? The outcome of a Pre-Approval Inspection (PAI) by any regulatory authority can lead to two potential recommendations at the conclusion of the inspection:

- Recommend Approval:
  - Indicates that the inspection found no significant issues.
- Recommend Withholding of Approval:
  - Indicates that the site is not GMP compliant, the information in the documentation is not consistent with site records or the submitted information is not accurate and complete.

Ultimately, the respective regulatory authority's decision-making body will make the final decision on whether to approve or withhold approval of the application or licensure



CPDS PAI GAP process audit

With the PAI GAP assessment the process is clear. Your submission is evaluated against the current QMS. The assessment methodology is standard:

- Meeting regulatory requirements
- Meeting your application data

Based on de US PAI program auditor instructions (available on our website), the focus of the assessment will be:

- Manufacturing processes documentation and controls
- Laboratory controls and data integrity
- Facility and equipment systems
- Material management systems
- Packaging and labeling systems
- Operational readiness for inspection preparation

Start the PAI preparation before submitting the file to the regulatory authority. Build a small team to evaluate your readiness, plan all corrections and improvements timely and work towards the PAI inspection.
We can support you as an external reference and provide further experience-based guidance.

Be prepared for audit practices like:

- Data Integrity Issues: One auditor requested from an analyst to open certain directories of the HPLC computer. He found various data that were not controlled as quality records, resulting in 483 observations for data integrity.
- Process Validation Issues: Another auditor positioned himself behind glass and closely observed one part of the aseptic filling line for over 14 hours across 3 days. He noticed breaches of first air while filling or interruptions, leading to several 483 observations for process validation.

These findings could have been prevented with a thorough preparation and validation. Make the PAI audit a success for your company. Be prepared, and remember, we can help. If you need further details or assistance, just let me know!

Post Inspection

If an external inspection results in Non-Conformities (NC), the investigation and response drafting should begin immediately. Here are key steps to follow:

- Document and Analyze Facts Promptly: Ensure the facts related to the findings are documented and analyzed the same day or by the next morning while all Subject Matter Experts (SMEs) and process owner specialists are still present.
- Thorough and Clear NC Responses: Your NC response and actions should be thorough and detailed enough for external reviewers who were not part of the audit to understand. Correct what you can immediately and include objective evidence.
- Reflect Your Quality Culture: The investigation should showcase your quality culture and thoroughness. Methods used should be referenced in the documentation.
- Complete Story in NC Responses: Ensure the response to the NC tells the full story. Anyone reading it should get a clear picture without having prior knowledge of the situation.

These steps will help ensure a comprehensive and effective response to any NCs identified during the inspection.

In summary:

- Begin response drafting immediately, even while investigating
- Include evidence of any corrections already completed
- Provide detailed timelines for actions you have planned
- Show root cause analysis methodology and findings
- Address the systemic-ness of each finding

Ensure you allocate sufficient resources to address the findings and bring them under control within a reasonable timeframe; otherwise a warning letter from the FDA (US) may be the result.

We, along with our staffing partner, can provide the expert team needed to help you achieve compliance and avoid negative outcomes.

Custom Service
This service will be tailored to your specific preferences. It can be delivered by one or several experts, all trained with the same methodology and policies. Expansion of the team will be performed in cooperation with preferred staffing agencies.
Contact us to discuss the possibilities.

Availability and Costs
The availability and costs of this service depend on the timing, type of inspection and remediation work.
Contact us for availability and pricing details.
If you have any other questions or need more information, feel free to reach out!

Languages
The service can be delivered in:
- English
- German
- Dutch

Duration
The duration of the service depends on your needs and preferences.
Contact us to discuss your specific requirements and tailor the service to your timeline and other preferences.

Benefits for Your Organization:
- Learn to transition into a lean cGMP, always-ready state.

Inspection Readiness: Preceding CPDS Modules:
Our four preceding CPDS modules lay the groundwork for achieving a state of readiness for inspections. These modules encompass various aspects such as:

- Developing a robust Quality Culture
- Enhancing Quality Management Maturity
- Implementing effective Quality Management Systems
- Conducting thorough GAP assessments
- Ensuring consistent documentation and data integrity
- Streamlining manufacturing and laboratory processes
- Training staff for inspection readiness

1. Initial Introduction Meeting (2 days)
This in-depth session is designed to understand your company's current status and specific needs. It forms the basis for designing the future state based on well-informed decisions.

By gaining a comprehensive understanding of your operations, processes, and challenges, we can tailor our approach to best support your journey towards inspection readiness and overall quality management improvement.

2. Gap Assessment
This comprehensive assessment will provide a broad review of the Pharma cGMP Quality Management System (QMS). The process will involve a detailed evaluation of your current systems and practices, leading to the creation of the necessary "process interaction map." This map will highlight how different processes interact within your QMS, identifying any gaps or areas for improvement.

By conducting this gap assessment, we can ensure your systems are robust, efficient and ready for any upcoming inspections.

3. CPDS Innovative Approach to Process Management

Discover CPDS's new methodology for managing processes effectively. Our innovative approach is designed to enhance the efficiency, robustness and maturity of your Quality Management System (QMS). This methodology focuses on:

- Streamlining processes to reduce complexity and improve clarity
- Implementing best practices for process control and optimization
- Ensuring data integrity and accurate documentation
- Enhancing communication and collaboration among process owners
- Continuously monitoring and improving process performance

By adopting CPDS's innovative approach, your organization can achieve a higher level of operational excellence and maintain a state of constant readiness for inspections.

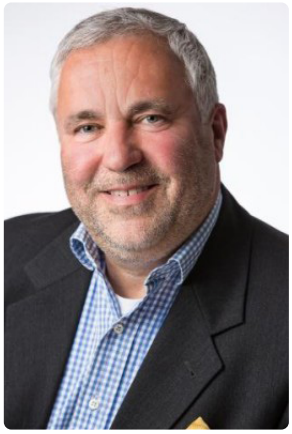
4. Write the Quality Manual with Quality Culture in Mind

Creating a cGMP/ISO manual that reflects your organization's Quality Culture is essential. This manual should serve as a comprehensive guide to your quality management principles, policies, and procedures.

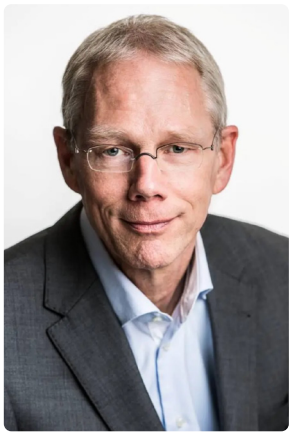
By completing these four modules, your organization will be well-prepared for any inspection, operating in a constant state of readiness and demonstrating a commitment to quality.

If you have any specific questions or need more details about these modules, feel free to reach out!

Readiness experts:



Rene van Melick PharmD



Dirkjan Bakker PhD

These experts bring extensive experience and knowledge to help ensure your organization is well-prepared for inspections and achieving compliance.

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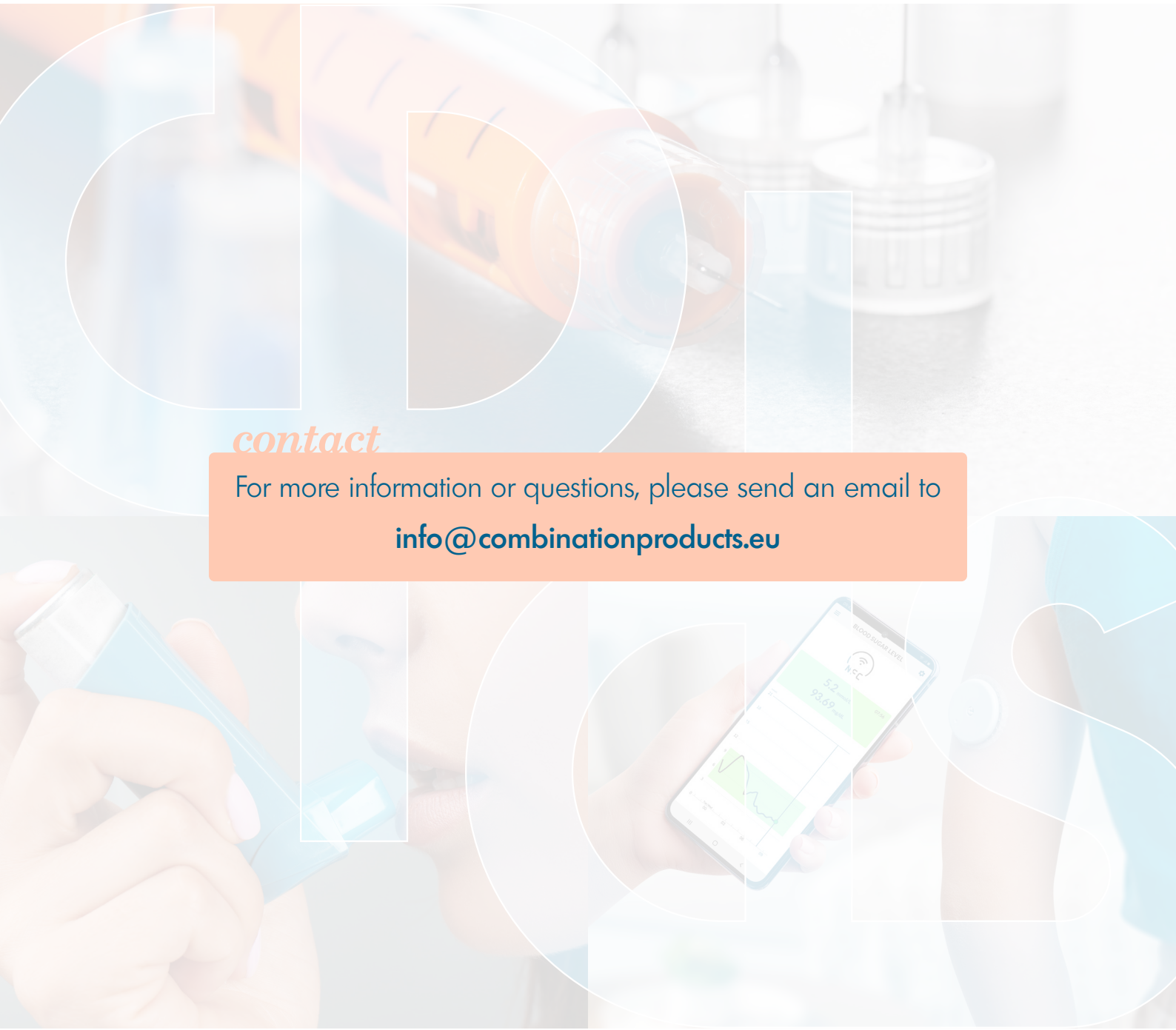

contact

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